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09/549,937	04/14/2000	Michael B Chancellor	2710-4007US2	9119

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EXAMINER
WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
1635	9

DATE MAILED: 05/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/549,937	CHANCELLOR ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-99* is/are pending in the application.

4a) Of the above claim(s) *4-16,28-44,56-83,85-91 and 97-99* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,17-27,45-55,84 and 92-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Non-Final Rejection

Claims 1-3, 17-27, 45-55, 84, 92-96 are pending.

Drawings

A correction to the drawings is required with response to this office action or the response will be considered non-responsive.

Information Disclosure Statement

The information disclosure filed on August 14, 2001 does not fully comply with the requirements of 37 CFR 1.98 because: applicant does not properly cite the journal article(s) listed on the 1449. Misspelling of the word "intraarticular" in the title of reference no. 25.

The examiner has considered all of the references, but in order to have the article listed above initialed and dated on the 1449, a new 1449 properly citing the article must be filed with the response to this office action. Failure to comply with this notice will result in the above mentioned information disclosure statement being placed in the application filed with the non-complying information not being considered. See 37 CFR 1.97(i).

Response to Election/Restriction

Applicants elected Group I (claims 1-3, 17-27, 45-55, 84, and 92-96) and species urological tissue in claim 17 and urinary sphincter tissue in claim 45 with traverse in paper no. 8.

The applicants argue that: Group I all pertain to novel muscle-derived used in method of the claimed invention; a search relating to the methods should encompass the several muscle

types for which the method is useful should not place an undue burden on the examiner. See pages 2-3.

Applicants' traversal is acknowledged and is found persuasive because after a search of the prior art, the methods are considered novel and the non-elected species are re-joined to the elected invention.

The restriction is deemed proper and is made final.

Claims 4-16, 28-44, 56-83, 85-91, and 97-99 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Specification

The specification contains misspellings of the word "be" on page 19, line 18. These and any other, spelling errors should be corrected in response to this office action. Applicant is encouraged to review the specification for additional spelling errors.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 17-27, 45-55, 84, and 92-96, as best understood, are readable on a genus of an isolated muscle derived progenitor cells having a long term survivability when introduced into mammals, wherein the cells express cell markers selected from the group consisting of at least

desmin, CD34, and Bcl-2, wherein the genus of the cells is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates a genus of an isolated muscle derived progenitor cells having a long term survivability when introduced into mammals, wherein the cells express cell markers selected from the group consisting of at least desmin, CD34, and Bcl-2. The as-filed specification provides sufficient description of a species of isolated cells from a mouse.

However, it is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or molecular structures of molecules that are essential for a genus of an isolated cells as claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or molecular structures of a genus of isolated muscle derived progenitor cells that must exhibit the disclosed biological functions as contemplated by the claims.

Furthermore, the disclosure does not provide an adequate written description of a representative number of species of isolated muscle-derived cells, which functions as intended in the claimed invention. It is not apparent from the specification that the description of phenotypic markers is essential for the biological function of the muscle-derived progenitor cells having long term survivability. The core structure that is required for an adequate description of a

representative number of species as embraced by the claimed genus of cells is not described sufficiently in the specification. As stated above, a mere statement asserting that any cell having the phenotypic markers without providing the essential elements (e.g. core structure) does not lend evidentiary support for a skilled artisan to have recognized that the applicant was in possession of the genus of cells having a phenotype as claimed, particularly since the skill and knowledge in the art is not adequate to determine the core structure of the representative number of species of muscle-derived progenitor cells that is essential for the biological function as intended by the claimed invention on the basis of the disclosure of only one species consisting of an isolated murine muscle-derived progenitor cells.

It is not sufficient to support the present claimed invention directed to a genus of isolated muscle derived progenitor cells. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming an unspecified genus of isolated cells that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision

the detailed structure of a genus of isolated muscle derived progenitor cells that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 1-3, 17-27, 45-55, 84, 92-96 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) Isolated murine muscle-derived progenitor cells, wherein the cells are pp6 and express cell markers selected from the group consisting of least desmin, CD34, Sca-1, Flk-1, and Bcl-2 and do not express CD45 and c-Kit; 2) Isolated clonal murine muscle-derived progenitor cells, wherein the clonally isolated cells express desmin, Flk-1, Sca-1 and does not express CD34, CD45, and c-Kit; and does not reasonably provide enablement for the entire breadth of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or the invention commensurate in scope with these claims.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Specifically, since the claimed invention is not supported by a sufficient written description (for possession of a genus of an isolated muscle-derived progenitor cells having long-term survivability) particularly in view of the reasons set forth above, one skilled in the art would not have known how to use and make the claimed invention so that it would operate as intended, e.g. for use in a method of augmenting or bulking muscle tissue in a mammal.

The state of the art for cell transplantation (e.g. myoblast) has been capable of delivering a protein (e.g. dystrophin) and improving muscle strength of injected muscle, this approach has been hindered by various limitations: immune rejection, poor cellular survival, and the limited spread of the injected cells (Lee et al., The Journal of Cellular Biology, Vol. 150, 2000, pp. 1085-1099). Lee further teaches:

> Skeletal muscle tissue has been extensively investigated as a potential source for isolation of pluripotent stem cells. A recent report has suggested that only a discrete minority of myoblast can survive after implantation and thus may represent a population of myogenic stem cells. In 1998, a specific population of highly purified muscle derived cells by the pre-plate technique that significantly improved cell survival after transplantation when injected intramuscularly. Although the mechanism by which these specific muscle derived cells display a high cell survival is unclear (page 1086).
> Comparison of the muscle-derived cells to other types of muscle-derived cells indicates that more studies are required to accurately assess the origin and more importantly, the functional property of these various populations of muscle-derived stem cells (page 1096-1097).

In addition, the state of the art teaches that "the study of muscle satellite cells as a stem cell and it role in skeletal muscle is still in its infancy and it will now be important to characterize the influence of growth factors and components of the extracellular matrix responsible for activating genetic responses within stem cells (Seale et al., Developmental Biology, 2000, page 122, IDS).

The specification provides working examples described below:

Example 1 teaches the preparation of mouse muscle derived cells (MDC), pp6 (pages 28-30). Examples 3-5 and 7-8 display that genetically modified MDC with Lac Z were viable for up to 4 weeks in the lower abdomen of rats as shown in Example 3 (pages 32-33 and 39-40). Example 6 displays an increase in the contraction amplitude and contraction velocity of bladder strips of

cryodamaged bladder tissue in rats using MDC (pages 33-39). Example 9 displays that genetically modified mc13 cells with adBMP-2 can cause bone formation (pages 40-51).

In view of the In re Wands Factors, the disclosure provides sufficient guidance for one skilled in the art to make murine cells pp6 and the clonal muscle-derived cells, mc13. However, in of the lack sufficient description provided by the specification for the genus of muscle-derived cells and the art of record further supporting this by stating that the functional properties of the various populations of muscle-derived cells require further research (Lee, pages 1096-1097); it is not apparent if cells from a different species with the same phenotypic markers would exhibit the same mechanisms because of the different markers displayed by other species. The specification and art of record teach that pp6 express Flk-1, which is a mouse homologue of human KDR gene (page 15). The art of record further teaches that:

> The expression of CD34 is reversible on hematopoietic stem cells. In fact, the art suggest that CD34 is probably a marker of activated stem cells, but it is not necessarily expressed in all stem cells. Although the reversible expression of CD34 remains to be determined in muscle derived stem cells, the use of CD34 as a marker of muscle-derived stem cells should at least by used with caution. Cells isolated at pp2 in our experiments are highly different than the cells isolated at pp6 in term of marker expression in vitro as well as their functional properties in vivo, see Qu et al., 1998, IDS (Lee et al, page 1096).
>
> Progenitor cells give rise to related types of cells-lymphocytes, such as T cells, B cells, and natural killer cells, for example-but in their normal state do not generate a wide variety of cell type as such are not truly stem cells. It is necessary to show that the adult stem cell give rise to cell types that normally occur in different tissue. Neither of these criteria are easily met. (http:/www.nih.gov.news/stemcell/scireport.htm, Executive Summary, ES-3, Appendix D, D-11 and D-12, and Chapter 4, page 23-25, 36, and 38).

In view of the specification and art of record it appears that the pp6 cells have different markers than other species, therefore, the cells would not be in other species. Thus, in view of the In re Wands Factors, it would require an undue amount of experimentation for one skilled the art to

reasonably extrapolate from making and using the cell from the mouse in the claimed invention to any other cell from a different species.

In addition, it is not apparent how an increase in the contractility of cryodamaged bladder tissue in rats using MDC reasonably correlates to a method of treating weakness or dysfunction in muscle tissue in mice using muscle derived cell therapy. The state of the art and the disclosure do not provide sufficient guidance for one skilled in the art to reasonably extrapolate for the use of the claimed invention in any species or in any type of weakness or dysfunction in muscle tissue because it is not apparent that an increase in the contraction amplitude and contraction velocity are accepted parameters for reasonably correlating to any therapeutic method set forth in the claimed invention. The specification fails to provide teaching what would be the appropriate dose of muscle-derived cells per route of administration for a sustained and high enough level of expression of transplanted cells in any species. In addition, it would be apparent to one skilled in the art that the addition of cells to the bladder would result in an increase of contraction amplitude due to the increase of muscle derived cells in the bladder strips. Also, the specification does not demonstrate directly or incorporate by reference, that the exemplified rat model is standard in the art for reasonably extrapolating cell transplantation results in rats to any other species and for any type of muscle weakness or dysfunction. At the time the application was filed, Kasemkijwattana et al. (IDS, Cell Transplantation, 1998) discloses that although muscle injury is capable of healing, an incomplete functional recovery often occurs (abstract) and the best treatment for muscle injury has not yet been define and the recommended treatment regimens for contusions have varied widely, depending on the severity of the injury (page 585). Furthermore, Ledley, *Pharmaceutical Research*, Vol. 13, pp. 1595-

1614, 1996, discloses that "while transplantation of hepatocytes, pancreatic cells, myoblasts, epidermal cells, neuronal cells, synovial cells, and fibroblasts has been demonstrated in animals, these methods are not routinely available for treating any medical disease or disorder in any mammal including humans (page 1596)." In addition, in the absence of assays demonstrating muscle function, and the failure of the specification to disclose that an increase in contractility of bladder strips from cryodamaged bladder in tissue in rats, and the increased production of fibers is at a sufficiently high enough level so as to result in an increase in muscle tissue function, then the disclosure fails to provide an enabling disclosure for the claimed invention to restore muscle or tissue function. Therefore, in the absence of essential teachings specific to the administration of muscle derived cells, it would require an undue amount of experimentation for one skilled in the art to reasonably extrapolate from the disclosure to the treatment of any type of muscle weakness or dysfunction in any species.

In addition, with respect to claims 17-27, 45-55, and 92-93, one skilled in the art would reasonably determine that the cells could not be used in different species (e.g. monkey, human, dog, etc.) because of the problem with exposing an animal to foreign cells (e.g. mouse cells) because of the differences in the immune system of a mouse compared to another species (e.g. human, monkey, etc.). The state of the art taught by Kuby displays that the degree of immune response to a graft caries with the type of graft (*Immunology*, 2nd edition, page 560, 1994). Kuby teaches that:

> Allografts are grafts between genetically different members of the same species. Because an allograft is genetically dissimilar to the host, it is often recognized as foreign by the immune system and is rejected in an allograft rejection (page 560). Xenografts are grafts between different species such as the graft of a baboon heart to a human (page 560). Xenografts exhibit the greatest genetic disparity and therefore engender the most vigorous graft rejection (page 560).

In addition, the specification lacks sufficient guidance for how to use any type of cells for augmenting or bulking muscle tissue in any mammal other than mouse, when the immune system of a mammal is exposed to xenogenic cells. This is an important factor with regard to a treatment regimen, which intends to use a source of functional and potentially immunogenic cells. In addition, the as-filed specification does not teach how to prevent host vs. graft rejection and/or graft vs. host rejection disease (GVHD) in any mammal being treated with a composition comprising cells from a different species (e.g. mouse) for use in a different mammal (monkey, human, dog, etc.). Furthermore, one skilled in the art understands the differences in major histocompatibility complex (MHC) human leukocyte antigens (HLA) in humans, between donor and recipient are the major mechanism of graft rejection. In addition, HLA are highly polymorphic, which makes it difficult to find donors. Moreover, even with a complete match for HLA graft rejection still takes place due to the incompatibility of minor histocompatibility antigens between donor and recipient. The specification fails to provide sufficient guidance for how one skilled in the art would be able to use any xenogenic cells without avoiding a GVHD or graft rejection.

In addition with respect to the concerns stated above encompassing the specific immune response in muscle derived cell transplantation, the prior art and specification do not provide sufficient guidance for one skilled in the art to use any type of muscle-derived cells. It is not apparent from the specification what type of pp6 cells were being used in the working examples (*e.g.* allogenic). The state of the art for myoblast transplantation as taught by Tremblay et al. *Basic. Appl. Myol.* Vol. 7, page 221-223, 1997 teaches that:

> The potential role of the immune system in myoblast transplantation has been largely underestimated. Many research groups have shown even before clinical trials that myoblast do express MHC. Transplantation of human myoblast in immunocompetent mdx mice has never been successful in my laboratory. Xenotransplantation has so far never been successful with or without immunosuppression even for organ transplantation. There was evidence of poor survival of MHC-matched muscle transplantation in immuno- competent animals. The importance of the specific immune response in the limited success of human myoblast transplantation was demonstrated by transplanting with great success human myoblast in immunodeficient SCID mice, which have no T and no B-lymphocytes. Because these mice are unable to reject transplanted tissues even from different species. Our research group obtained good evidence of cellular rejection following MHC incompatible allo- and xenotransplantation of myoblasts in immunocompetent mice not immunosuppressed. Myoblast obtained from MHC compatible mice, but from a strain different from the host, were also rejected by immunocompetent hosts. Rejection of myoblast transplantation can still be due to MHC or minor antigens unless an adequate immunosuppression is used. Myoblasts transplantation in immunocompetent animals is definitively very immunogenic.

Furthermore, it is apparent from the as-filed specification and the state of the art that an immunosuppressive regimen is required to avoid an immune response in immunocompetent animals transplanted with MDCs. However, the claims do not encompass using any type of immunosuppressive regimen. Also, as stated above, the claims read on using any type of muscle-derived cells (*e.g.* xenogenic). In view of the state of the art and the lack of sufficient guidance provided by the disclosure it would take an undue amount of experimentation to determine what type of MDC (*e.g.* xenogenic) would avoid rejection by the animal's immune system following transplantation of MDC into said animal. Thus, even if the as-filed specification displays working examples of MDC transplantation in experimental rats using unspecified pp6 cells, it would require an undue amount of experimentation to reasonably correlate MDC transplantation in rats to muscle derived transplantation in any other mammal in view of the doubts expressed in the art of record for muscle derived cell transplantation and/or the lack of sufficient guidance provided by the specification and/or given there is no evidence

that the working examples using rats is a general phenomenon. Thus, one skilled in the art could not predict with a reasonable degree of certainty that the claimed murine cells could be used successfully for a therapeutic use for treating weakness or dysfunction in muscle tissue or augmenting or bulking muscle tissue, especially since there are no universal examples of using xenogenic cells in the specification or in the prior art. Thus, the specification is only enabled for producing murine muscle-derived progenitor cells.

Furthermore, if the applicants are able to provide sufficient guidance or factual evidence to overcome the concerns under 112 written description and enablement set forth above, the specification does not provide sufficient guidance for one skilled in the art to reasonably extrapolate the working examples in the specification to a method of augmenting or bulking bladder tissue to any other method of augmenting or bulking muscle tissue and/or any other method of treating weakness or dysfunction in muscle tissue in any mammal because of the art of record (e.g. http:/www.nih.gov.news/stemcell/scireport.htm) and the differences between smooth and skeletal muscle in a mammal (Martini et al., Fundamentals of Anatomy and Physiology, Prentice Hall, Inc., 3rd edition, 1995, page 315). The art of record displays the unpredictability of muscle-derived cells differentiating into a specific muscle tissue. In addition, the as-filed specification or the state of the art do not provide sufficient guidance or factual evidence for one skilled in the art to reasonably extrapolate from the working examples in the specification to any other type of muscle because of the lack of evidence showing that the working example in the specification is a general phenomenon, and given the doubts expressed in the art of record. Therefore, it would require an undue amount of experimentation for one skilled in the art to practice the full breadth of the claimed invention..

In conclusion, the as-filed specification and claims coupled with the state of the art at the time the invention was made only provide sufficient guidance and/or evidence to reasonably enable the claimed invention 1-2, listed above. One skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the application's disclosure, the unpredictability of cells with any phenotype selected from the group consisting of desmin, CD34, Bcl-2 and Sca-1 or Flk-1.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 84, and 94 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 84 is vague and indefinite because step d refers to the cells of step (c) and it is not apparent whether the cells are the non-adherent or adherent cells. The disclosure does not define which cells are being claimed. Clarification is requested.

The term "long-term survivability" in claims 1 and 94 is a relative term, which renders the claim indefinite. The term "long-term survivability" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The disclosure does not define the metes and bounds of the term. It is not apparent what time period (4 weeks, 6 months, 10 years, etc.) is being defined by the claims or being compared to.

Double Patenting

The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper time-wise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 84, and 94-95 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 76-80 of co-pending Application No. 09/302,896. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of co-pending application '896 are drawn to a method of isolating and purifying muscle-derived stem cells, comprising: a) plating dissociated muscle cells on a collagen-coated substrate; b) isolating muscle derived cells populations which adhere to said substrate at successive time intervals following said plating step a); and c) determining the characteristics of the isolated cell population to identify muscle-derived stem cells (claim 76). In addition, the claims are drawn to the method described above, wherein said cells express one or more markers selected from BCL-2, CD34, and desmin (claim 79).

Although the conflicting claims in the instant application and co-pending application '896 are not identical, they are not patentably distinct from each other because each invention encompasses the same material and the patents use the muscle derived cells encompassed in the

instant application. The difference between the claims of the instant application and co-pending application '896 is that the instant application encompasses more descriptive steps of the isolation process of muscle-derived cells. Therefore, the claims of the instant application and co-pending application '896 are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 84, and 94-95 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over co-pending Application No. 09/302,896, which has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the co-pending application, it would constitute prior art under 35 U.S.C. 102(e) if published or patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future publication or patenting of the conflicting application. Co-pending application '896 has claims, which encompass a method of isolating and purifying muscle derived stem cells, wherein the cells express one or more markers selected from the group consisting of desmin, CD34, BCL-2 (claims 76-80).

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the co-pending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the co-pending application under 37 CFR 1.131. For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kay Pinkney whose telephone number is (703) 305-3553.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, primary examiner, Dave Nguyen can be reached at (703) 305-2024.

If attempts to reach the primary examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-7939.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0198.

Brian Whiteman
Patent Examiner, Group 1635
5/19/02

DAVE T. NGUYEN
PRIMARY EXAMINER